

Tenofovir



Drug Class: Microbicides

Drug Description

Tenofovir is an adenosine nucleoside monophosphate reverse transcriptase inhibitor and viral replication inhibitor. [1]

HIV/AIDS-Related Uses

Tenofovir gel, also known as PMPA gel, is being investigated in Phase II monotherapy studies as a vaginal microbicide for the prevention of HIV transmission. Tenofovir is also being studied in combination with PRO 2000, another investigational vaginal microbicide.[2] [3] Approved oral formulations of its prodrug, tenofovir disoproxil fumarate (tenofovir DF), are used to treat HIV.[4]

Non-HIV/AIDS-Related Uses

In vitro testing of tenofovir demonstrated antiviral activity against hepatitis B virus (HBV).[5] Tenofovir disoproxil fumarate, the orally bioavailable prodrug of tenofovir, is being evaluated in HBV/HIV co-infected patients who developed HBV breakthrough during treatment with lamivudine.[6]

Pharmacology

Tenofovir, a nucleotide analogue, is characterized by its ability to enter and inhibit viral replication in HIV infected, HIV uninfected, and resting cells, thus forming active drug reservoirs.[7]

Tenofovir has a long intracellular half-life.[8] Serum plasma concentrations with tenofovir gel application have ranged from 3 to 25.8 ng/ml, remaining lower than the 50 ng/ml minimum plasma concentration achieved with oral tenofovir DF.[9]

Animal studies support the use of tenofovir gel as a microbicide. One small study of tenofovir gel administered vaginally to four macaques resulted in 100% protection, compared with observed HIV transmission in two macaques administered placebo gel.[10]

HPTN 050, an open-label, Phase I trial, evaluated tenofovir 0.3% and 1% gels, administered daily or twice-daily for 2 weeks in sexually abstinent HIV infected and HIV uninfected women to determine toxicity, pharmacokinetics, and gel acceptability. Fourteen of 25 women (56%) experienced low but detectable serum tenofovir levels. Asymptomatic bacterial vaginosis in 29 women resolved in 14 (48%) after gel administration. No new resistance mutations evolved, and no patients had high-level tenofovir mutations, such as K65R.[11] [12]

HPTN 059 is an ongoing, multicenter, randomized, Phase II trial in HIV uninfected women to determine the safety and acceptability of tenofovir 1% gel administered over 24 weeks with a 48-week follow-up. Patients will be assigned to one of four cohorts: tenofovir 1% daily; placebo daily; tenofovir 1%, coitally dependent; or placebo, coitally dependent.[13]

Adverse Events/Toxicity

In an open-label, Phase I trial to evaluate tenofovir 0.3% and 1% gel concentrations in HIV uninfected and HIV infected women, the gel was well tolerated. Although 92% of patients experienced at least one adverse effect, 87% were mild and 70% were genitourinary. Thirty-two percent of patients experienced gastrointestinal effects. One severe adverse effect, lower abdominal cramping, was considered possibly drug-related.[14]

The most common adverse effects noted were itching (23%), redness (18%), discharge (15%), irregular menstruation (13%), and uterine bleeding (11%). Vaginal candidiasis occurred in 5% of women while using the gel.[15]

In irritation studies, tenofovir 0.3% and 1% gels, adjusted to pH 4 to 5, appear nearly equal to carrier vehicles in irritation scores.[16]

Clinical Trials

For information on clinical trials that involve Tenofovir, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Tenofovir AND HIV Infections.

Tenofovir



Dosing Information

Mode of Delivery: Intravaginal.[17]

Dosage Form: Tenofovir gel is available in 0.3% and 1% concentrations. In clinical studies, it is applied vaginally once or twice daily. Precoital applications are also being investigated.[18]

Tenofovir gel is packaged in 6-gram tubes and in 4-gram, single-dose applicators.[19]

Chemistry

CAS Name: Phosphonic acid,

Tenofovir



Chemistry (cont.)

CAS Number: 147127-20-6[21]

Molecular formula: C₉H₁₄N₅O₄P[22]

C37.64%, H4.91%, N24.38%, O22.28%,
P10.78%[23]

Molecular weight: 287.21[24]

Melting point: 279 C[25]

Physical Description: Clear, transparent, viscous
gel.[26]

Other Names

GS-1275[27]

PMPA gel[28]

(R)-9-(2-Phosphonomethoxypropyl)adenine[29]

(R)-9-(Phosphonomethoxypropyl)adenine[30]

Tenofovir



Other Names (cont.)

Further Reading

Tenofovir gel studied. AIDS Patient Care STDS. 2002 Aug;16(8):401-2.

D'Cruz OJ, Uckun FM. Clinical development of microbicides for the prevention of HIV infection. Curr Pharm Des. 2004;10(3):315-36.

Meyer KH, Maslankowski LA, Gai F, El-Sadr WM, Justman J, Kwiecien A, Masse B, Eshleman SH, Hendrix C, Morrow K, Rooney JF, Soto-Torres L; HPTN 050 Protocol Team. Safety and tolerability of tenofovir vaginal gel in abstinent and sexually active HIV-infected and uninfected women. AIDS 2006 Feb 28;20(4):543-551.

Manufacturer Information

Tenofovir
Gilead Sciences Inc
333 Lakeside Dr
Foster City, CA 94404
(800) 445-3235

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

1. Curr Pharm Des - 2004;10(3):315-36
2. Treatment Action Group - Microbicides Pipeline - Table 2. Available at: <http://aidsinfo.org/tag/science/immunePipelineTables.html>. Accessed 01/30/07.
3. AIDS - 2006 Feb 26;20(4): 543-51
4. Gilead Sciences - Investors: News Releases. Gilead Announces Initiation of NIH-sponsored Phase I Trial to Evaluate Tenofovir Topical Gel as Preventive for Vaginal Transmission of HIV [press release], May 21, 2002. Available at: http://www.gilead.com/wt/sec/pr_298978. Accessed 01/30/07.
5. Infection - 2006 Aug;34(4):234-5
6. AIDS Patient Care STDS - 2006 Dec;20(12):517-22
7. Gilead Sciences - Investors: News Releases. Gilead Announces Initiation of NIH-sponsored Phase I Trial to Evaluate Tenofovir Topical Gel as Preventive for Vaginal Transmission of HIV [press release], May 21, 2002. Available at: http://www.gilead.com/wt/sec/pr_298978. Accessed 01/30/07.
8. Gilead Sciences - Investors: News Releases. Gilead Announces Initiation of NIH-sponsored Phase I Trial to Evaluate Tenofovir Topical Gel as Preventive for Vaginal Transmission of HIV [press release], May 21, 2002. Available at: http://www.gilead.com/wt/sec/pr_298978. Accessed 01/30/07.
9. AIDS - 2006 Feb 26;20(4):543-51
10. Conf Retroviruses Opportunistic Infect - 13th, 2006. Abstract 569.
11. Gilead Sciences - Investors: News Releases. Gilead Announces Initiation of NIH-sponsored Phase I Trial to Evaluate Tenofovir Topical Gel as Preventive for Vaginal Transmission of HIV [press release], May 21, 2002. Available at: http://www.gilead.com/wt/sec/pr_298978. Accessed 01/30/07.
12. AIDS - 2006 Feb 26;20(4):543-51
13. HPTN - Phase II Expanded Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel. Available at: http://www.hptn.org/research_studies/hptn059.asp. Accessed 01/30/07.
14. AIDS - 2006 Feb 26;20(4): 543-51
15. AIDS - 2006 Feb 26;20(4): 543-51
16. AIDS - 2006 Feb 26;20(4): 543-51
17. AIDS - 2006 Feb 26;20(4): 543-51
18. AIDS - 2006 Feb 26;20(4): 543-51
19. AIDS - 2006 Feb 26;20(4): 543-51
20. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 01/30/07.
21. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemlite.jsp>. Accessed 01/30/07.
22. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 01/30/07.
23. Merck Index - 2006, p. 1573
24. Merck Index - 2006, p. 1573
25. Merck Index - 2006, p. 1573
26. AIDS - 2006 Feb 26;20(4): 543-51
27. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 01/30/07.
28. AIDS - 2006 Feb 26;20(4):543-551
29. ChemIDplus - Availabel at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 01/30/07.

Tenofovir



30. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 01/30/07.
31. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 01/30/07.